

REMARKS

Upon entry of this amendment, claims 1-10, 13-33, and 36-50 are pending in the instant application. Among them, claims 14, 16-29, and 37-42 are withdrawn from consideration as being drawn to non-elected inventions. Applicants will cancel these claims upon indication of allowable subject matter. Claims 1-10, 13, 15, 30-33, 36, 43, and 44, and new claims 45-50 are currently under consideration.

The original Final Office Action was mailed on Nov. 2, 2001. Applicants have submitted evidence to show that the Office Action mailed on Nov. 2, 2001, was never received. Since a Notice of Abandonment was never mailed, the application is held to be pending (see Paper No. 12), and the Final Office Action was remailed on July 29, 2002. Accordingly, a three-month shortened statutory period for reply was set to expire on October 29, 2002.

Since the remailed Final Office Action was received on Aug. 2, 2002, the IDS filed by Applicants on Aug. 1, 2002, under 1.97(c) with the fee set forth in 37 CFR 1.17(p) was not considered by the Examiner. Applicants hereby resubmit a copy of the IDS form PTO/SB/08 under 37 CFR 1.97(b) with this Request for Continued Examination.

Applicants have added new claims 45-50 to further clarify the subject matter claimed. Support for these new claims can be found throughout the specification. For example, claim 45 is supported by p15, last paragraph. Claim 46 is supported by page 1, last paragraph. Claim 47 is supported by page 16, line 14 – page 17, line 6, also by Examples 8-10. Claim 48 is supported by Example 10. Claims 49-50 are supported by the paragraph bridging pages 19-20 and Example 1.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Double Patenting

Claims 1-10, 13, 15, 30-33, 36, 43 and 44 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Pat. No. 5,834,188. Without conceding the appropriateness of this rejection, Applicants will

submit a terminal disclaimer, if necessary, to obviate this rejection upon indication of allowable subject matter.

Claim rejections under 35 U.S.C. 112, first paragraph – Written Description

Claims 30-33 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Office Action alleges that only specific SEQ ID NOs. meet the written description requirement, while “species or allelic variants,” “truncated amino acid sequences,” “analog thereof,” etc. do not.

Applicants have amended claims 30 and 43 to clarify the subject matter claimed. Specifically, to expedite prosecution, Applicants have deleted “species or allelic variants,” “truncated amino acid sequences,” “analog thereof,” etc. to obviate the rejection. Applicants reserve the right to prosecute claims pertaining to such subject matter in future applications. Applicants have also amended claim 43 to clarify the subject matter claimed. Support can be found throughout the specification, such as on page 15, last paragraph. Applicants submit that these claims and their dependent claims meet the written description requirement. For example, sequences of OP-2, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, Vg1, Vgr-1, DPP, or 60A, though not explicitly disclosed in the instant application as SEQ ID NOs., were well known in the art at the time the application was filed (see the cited references). Applicants also submit that notwithstanding the removal of “species or allelic variants” etc., the claims plainly cover variations in sequence that do not substantially change the activity and overall properties of the recited morphogen.

Pursuant to MPEP 2164.05(a): “The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).” In addition, according to the *Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, ¶1, “Written Description” Requirement* (2000), F.R. 66(4): 1099-1111,

“an applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention... What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.”

Therefore, Applicants submit that all claims as amended meet the Written Description Requirement of 35 U.S.C. 112, first paragraph. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim rejections under 35 U.S.C. 112, first paragraph – Written Description

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being unclear.

Applicants have amended claim 44 to clarify the subject matter claimed, thereby obviating this rejection. Applicants submit that there is no narrowing of scope in any respect due to this amendment. Reconsideration and withdrawal of this rejection is respectfully requested.

Claim rejections under 35 U.S.C. 103(a)

Claims 1 and 13 are rejected under 35 U.S.C. 103(a), as being unpatentable over Foulkes et al. in view of Wobus et al.

Specifically, the Office Action alleges that Foulkes teaches a general method of identifying a compound that induces a biological effect, but does not teach a motivation to apply the method to differentiated mammalian tissue to identify chronotropic drugs which induce differentiation, while Wobus teaches a motivation to apply the Foulkes method to the identification of compounds to study differentiation. Applicants respectfully disagree for the reasons which follow.

First of all, Wobus is a research article titled “pluripotent mouse embryonic stem cells are able to differentiate into cardiomyocytes expressing chronotropic responses to adrenergic and cholinergic agents and Ca²⁺ channel blockers” (emphasis added). Thus, it is a study directed to

the differentiation of mouse ES cells to cardiac muscle cells (cardiomyocytes). The Office Action failed to show that differentiation of a cardiac muscle cells from ES cells actually is a “morphogen-mediated biological effect” as recited in the amended claim 1 (as well as in the original claim 1 as filed) or its dependent claim 47. In fact, the subject matter of Wobus is quite different from the subject matter as claimed, which is identification of compounds that can mimic the effects of morphogens in inducing a morphogen-mediated biological effect, such as expression of a differentiation marker protein collagen X, and those recited in claim 47.

The only remotely related aspect of Wobus and the instant application is differentiation. However, as stated above, the Office Action has failed to establish a nexus between cardiac muscle cell differentiation and a morphogen-mediated biological effect. Thus even if (for the sake of argument) a skilled artisan is motivated to combine the cited references, he would only arrive at a method of screening for chronotropic (meaning “something affecting the time or rate, as the rate of contraction, of the heart,” according to the On-line Medical Dictionary, **Exhibit A**) drugs, or other drugs having a biological effect of inducing cardiac muscle differentiation, none of which is what is claimed. It also logically follows that the skilled artisan would have no reasonable expectation of success in arriving at the claimed invention.

Pursuant to MPEP 2142, “To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).” (emphasis added).

Therefore, based on the above argument, at least two of the legal requirements to establish a *prima facie* case of obviousness are not met. Reconsideration and withdrawal of this rejection on ground of 35 USC 103(a) is respectfully requested.

Claims 1-3, 6, 9, 13, 30-33, 36, 43 and 44 are rejected under 35 U.S.C. 103(a), as being unpatentable over Foulkes et al. in view of Wobus et al. and further in view of Nadal-Ginard.

Specifically, the Office Action alleges that Foulkes teaches a general method of identifying a compound that induces a biological effect, the use of vectors with AP-1 sites, the production of large amounts of desirable compounds for therapeutic use, but does not teach the use of MEF-2 or AP-1 elements. Wobus allegedly teaches a motivation to apply the Foulkes method to the identification of compounds to study differentiation. And Nadal-Ginard allegedly teaches screening for agents that enhance or decrease the interaction of MEF-2, MyoD, and MASH transcriptional factors.

As argued above, even for the sake of argument, the combined teachings of Foulkes and Wobus relate to screening for drugs useful for cardiac muscle differentiation, or study of toxicology of chronotropic drugs. Both are fundamentally irrelevant to the claimed invention.

Nadal-Ginard relates to “screening procedures that identify agents for decreasing the proliferation of neoplastic cells, and agents for inducing the replication of cells in a terminally differentiated state.” (Page 1 of Nadal-Ginard). Thus, this subject matter is also fundamentally different from the claimed invention. The Office Action has failed to establish a connection between the claimed invention and that of the cited references. Particularly, amended claim 1 recites the requirement that “said morphogen-mediated biological effect requires the presence of said morphogen-responsive transcription activating element.” Therefore, even if the MEF-2 or other sites used in the Nadal-Ginard can be considered as “variants” of the MEF-2 sites of the claimed invention, in the absence of a showing that the biological effect is a “morphogen-mediated” one, and that the biological effect actually depends on the MEF-2 sequence, the subject matter of Nadal-Ginard remains different. The Office Action has failed to show either of these requirements. Thus, even assuming the teaching of Nadal-Ginard can be further combined with that of Foulkes and Wobus, it still would not correct the defect described above and allow a skilled artisan to arrive at the claimed invention. It also logically follows that a skilled artisan would have no reasonable expectation of success in arriving at the claimed invention even by combining all the cited references.

Therefore, based on the above argument, at least two of the legal requirements to establish a *prima facie* case of obviousness are not met. Reconsideration and withdrawal of this rejection on ground of 35 USC 103(a) is respectfully requested.

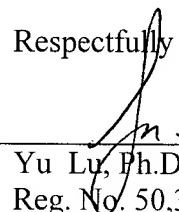
CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

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Respectfully Submitted,



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chronotropic

<pharmacology> Affecting the time or rate, as the rate of contraction of the heart.

Origin: Gr. Tropikos = turning

(18 Nov 1997)

Previous: [chronophobia](#), [chronophotograph](#), [chronospecies](#), [chronotaraxis](#), [chronotherapy](#)

Next: [chronotropism](#), [chroococals](#), [chrys-](#), [chrysanthemum-carboxylic acids](#)

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